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LETTERS TO THE EDITOR

Anemia and Poor Prognosis in Advanced Heart Failure

I read with great interest the study by Horwich et al. (1) on the association of anemia with poor prognosis in advanced heart failure. The investigators observed that mortality decreased in linear fashion as hemoglobin level increased without excess mortality at the highest hemoglobin level. However, hemoglobin level >17 g/dl was seen in only 3% of men and 1% of women. Thus, the small number of patients at high hemoglobin level could have limited the investigators' ability to observe a U-shaped relationship.

The percentage of patients with chronic obstructive lung disease who are the most likely candidates to have high hemoglobin were not listed in the report. I would appreciate the investigators' comments.

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REFERENCE

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REPLY

We appreciate Dr. Ghali's interest in our recent investigation of the relationship between hemoglobin (Hb) level and mortality in patients with advanced heart failure (HF) (1). We fully agree with Dr. Ghali that our ability to detect excess mortality in HF patients with above-normal Hb levels is limited by the small number of patients in this population. The issue of optimal Hb levels in HF and the possibility of a U-shaped relationship with regard to mortality is increasingly important, as interest grows in correcting anemia in HF using erythropoietin or newer analogues.

Prospective epidemiological studies such as the Framingham Heart Study have demonstrated a U-shaped relationship between hematocrit and mortality due to cardiovascular disease (2). A preliminary analysis of elderly patients with mild to moderate HF enrolled in the Evaluation of Losartan In The Elderly (ELITE) II study showed a U-shaped relationship, with higher mortality seen in men with hemoglobin levels >16.5 g/dl and in women with hemoglobin levels >15.5 g/dl (3). It is interesting to note, however, that an analysis of patients with mild to moderate HF in the Studies Of Left Ventricular Dysfunction (SOLVD) database failed to find a U-shaped relationship between hematocrit and mortality in HF (4). Male patients with a hematocrit of 40% to 49% (n = 4,235) had a mortality rate similar to those with hematocrit levels above 50% (n = 344).

As Dr. Ghali points out, the highest Hb level would be expected in patients with severe chronic obstructive pulmonary disease (COPD). Unfortunately, we do not have data on rates of COPD in our cohort, as it was not a variable in our original study design. In our study and the analysis of the SOLVD database, only a small proportion of patients with HF had elevated hemoglobin or hematocrit levels. Analyses of HF populations that include patients with increased Hb levels secondary to COPD, congenital heart disease, or polycythemia vera would make assigning relative mortality risk of elevated Hb versus the primary disease process leading to increased hemoglobin extremely difficult.

Initial reports on using erythropoietin in mild to moderately anemic HF patients in order to raise Hb to at least 12.5 g/dl have shown clinical benefit and no adverse effects (5). Conversely, a randomized controlled trial in 1,233 patients with HF or ischemic heart disease along with renal failure on hemodialysis showed a trend for increased cardiovascular events in subjects randomized to maintain a hemoglobin of 14 g/dl compared to those with a goal of 10 g/dl (6). Further clinical trials are needed to definitively assess whether raising hemoglobin is beneficial in HF and whether there is an upper limit of hemoglobin level above which benefit is lost.

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Use of Term "Non-Q Infarction" is Questioned

The recent study in *JACC* titled "Revisiting the Culprit Lesion in Non–Q-Wave Myocardial Infarction" warrants comment (1). The